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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/584,249	06/23/2006	Tomoyoshi Ishikawa	081356-0261	1542

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EXAMINER	
KIM, YUNSOO	

ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/584,249	ISHIKAWA ET AL.	
	Examiner	Art Unit	
	YUNSOO KIM	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 February 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14 and 16-23* is/are pending in the application.

4a) Of the above claim(s) *22 and 23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14 and 16-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/3/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-14 and 16-23 are pending.

Claims 22-23 stand withdrawn from further consideration by the examiner under 37CFR 1.142(b) as being drawn to a nonelected invention.

Claims 1-14 and 16-21 drawn to a stable liquid medical formulation are under consideration in the instant application.

2. Applicant's IDS filed on 2/3/09 is acknowledged.

3. In light of Applicants' amendments to the claims filed on 2/3/09, the following rejections remain.

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office Action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 1-14 and 17-21 stand rejected under 35 U.S.C. 103 as being unpatentable over U.S. Pat. No. 6,171,586B1, of record in view of U.S. Pat. No. 5,677,165, of record, for the reasons set forth in the office action mailed on 9/4/08.

The '586 patent teaches a stable aqueous pharmaceutical antibody formulation comprising an antibody in a citrate buffer at pH 4.5-6 (col. 6, lines 61-col. 7, lines 3, col. 5, lines 50-65). The '586 patent teaches the formulation prefers no addition of NaCl (col. 22, lines 31-35), but prefers addition of sorbitol as an isotonizing agent (e.g. tonifier, col. 6, line 52) and addition of polysorbate 80 as a surfactant (col. 22, lines 49-55). The referenced term "pharmaceutical" is interpreted to mean the claimed "medical".

Moreover, the '586 patent teaches the antibody is humanized, monoclonal antibody or chimeric antibody (col. 13-17). Claims 13-14 are included in this rejection as the purification methods of said antibody differentiate IgG1-4 and the resultant antibodies are IgG1-4 (col. 21, lines 41-65). The '586 patent further teaches the use of EDTA as a stabilizer (col. 23, lines 11).

The '586 patent teaches that the antibody formulation comprising a buffer, surfactant and stabilizer improves stability (col. 1, lines 15-40, col. 5-6, overlapping paragraph) and this formulation works for antibody formulation of various antigen targets (col. 10, lines 5- col. 11, lines 14).

Furthermore, the '586 patent teaches that the buffer concentration is 1-50mM (col. 22, line 26), the concentration of the antibody is 2mg/ml to 10 mg/ml (col. 22, line 16), the concentration of surfactant (polysorbate 80) is 0.01% (col. 22, lines 49-60) and the osmotic pressure is between 250mOsm and 350mOsm (col. 6, lines 32-36). The percent concentration of 1g/100ml is 1%, the 0.01% of polysorbate 80 is equivalent to 0.1mg/ml.

The disclosure of the '586 patent differs from the claimed invention in that it does not teach use of glutamate as in claims 1, 19-20 and the use of CD-40 antibody as in claim 17.

The '165 patent teaches the antibody specific to CD40 and addition of glutamate in other buffer system to minimize pH change (col. 7, lines 41-50).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to add glutamate and employ CD40 antibody as taught by the '165 patent to the antibody formulation taught by the '586 patent.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because the substitution of the CD-40 antibody to the antibody formulation taught by the '586 patent improves overall stability of the antibody and the addition of glutamate into other buffer system minimizes the pH change of the antibody solution.

From the teachings of references, it would have been obvious to one of ordinary skill in art to combine the teachings of the references and there would have been a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary in the art at the time of invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicants' arguments filed on 2/3/09 have been fully considered but they are not persuasive.

Applicants have argued that the '165 patent discloses a citrate buffer as the most preferred and there is no motivation for selecting a glutamate from the subgenus of the buffer choices according MPEP2144.08(II)(4).

Contrary to applicant's assertion, the '165 patent discloses citrate, phosphate, succinate, glutamate buffers and mixtures thereof (col. 7, lines 43-45) as a preferred buffer. Note that the claimed composition is not limited to a formulation consisting of an antibody and a glutamate. Rather, the term "contains" is considered open as "comprising" and the claimed formulation allows addition of other buffer, stabilizers and/or excipients.

Applicants have argued that the burden to show prima facie obviousness based on MPEP 2144.08(II)(4) remains to the examiner. However, the '586 patent discloses that phosphate buffer is not suitable for an antibody formulation that is subject to freeze/thaw (col. 7, line 4). Given that the combination of buffer is allowed and citrate is already taught in the '586 patent, the subgenus of buffers in the '165 patent are succinate and glutamate.

Note that MPEP 2144.08 (II) (4)(b) states:

> If the prior art reference expressly teaches a particular reason to select the claimed species or subgenus, Office personnel should point out the express disclosure which would have been motivated one of ordinary skill in the art to select the claimed invention. An express teaching may be based on a statement in the prior art reference such as an art recognized equivalence. See also, In re Kemps, 97 F. 3d 1427, 1430, 40 USPQ2d 1309, 1312 (Fed. Cir 1996) (holding there is sufficient motivation to combine teachings of prior art to achieve claimed invention where one reference specifically refers to the other).

Given the examination guidelines for determining obviousness under 35 U.S.C. 103 in view of the Supreme Court decision in *KSR International Co. v. Teleflex Inc.* 82 USPQ2d 1385 (2007) and the Examination Guidelines set forth in the Federal Register (Vol. 72, No. 195, October 10, 2007) and incorporated recently into the MPEP (Revision 6, September 2007), the following rationales to support rejection under 35 U.S.C. 103(a) are noted:

"Obvious to try" --- choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success.

The rationale to support a conclusion that the claim would have been obvious is that a person of ordinary skill has good reason to pursue the known options (succinate or glutamate) within his or her technical grasp. This leads to the anticipated success of enhancement of stability of the antibody formulation, it is likely the product not of innovation but of ordinary skill and common sense. Therefore, the combination of references remains obvious.

6. Claim 16 stand rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Pat. No. 6,171,586 B1, of record, and U.S. Pat. No. 5,677,165, of record as applied to claims 1-14, 17-21 above, and further in view of U.S. Pat. 6,416,958B2, of record, for the reasons set forth in the office action mailed 9/4/08.

The '586 patent and the '165 patent have been discussed, supra.

The disclosures of the '586 and 165 patents differ from the claimed invention in that they do not teach the use of HLA-DR antibody as in claim 17 of the instant application.

The '958 patent teaches a therapeutic composition comprising a HLA-DR antibody (col. 11, lines 35-54).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ the stabilizing formation taught by the '586 patent and the '156 patent into a HLA-DR antibody taught by the '958 patent.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because the formulation taught by the '586 patent and the '165 patent improve stability of the antibody formulation and minimize pH change.

From the teachings of references, it would have been obvious to one of ordinary skill in art to combine the teachings of the references and there would have been a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of the ordinary in the art at the time of invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicants' arguments filed on 2/3/09 have been fully considered but they are not persuasive.

Applicants have argued that the '165 patent discloses a citrate buffer as the most preferred and there is no motivation for selecting a glutamate from the subgenus of the buffer choices according MPEP 2144.08(II)(4).

In light of discussion in section 5 of this office action, the combination of references remains obvious.

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

8. No claims are allowable.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to YUNSOO KIM whose telephone number is (571)272-3176. The examiner can normally be reached on M-F,9-5. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen B. O'Hara can be reached on 571-272-0878. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Yunsoo Kim
Patent Examiner
Technology Center 1600
April 3, 2009

/Michael Szperka/
Primary Examiner, Art Unit 1644